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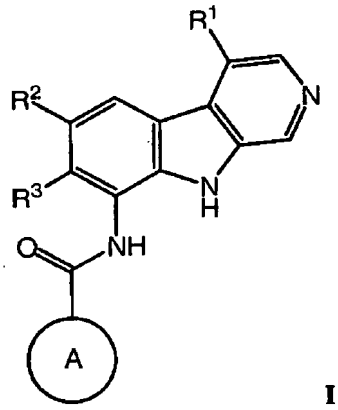
In the Claims:

Please cancel claims 2-8, 10-16, 18, 26, and 27.

1. (Currently Amended) A compound of formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

Ring A is ~~selected from the group consisting of:~~

~~(a) a pyridinyl or pyrimidinyl ring that is substituted by (i) $-CH_2C(O)$-G and 0-1 R^{6a} or (ii) 1-2 R^{6a}, and~~

~~(b)~~ a morpholinyl~~, piperidinyl, piperazinyl, pyrrolidinyl, pyranyl, tetrahydrofuranyl, cyclohexyl, cyclopentyl or thiomorpholinyl~~ ring that is substituted by (i) $-C(R^9)_3$, –W-G, or –G, (ii) 0-4 R^{6b} and (iii) 0-1 oxo groups on a ring carbon or 0-2 oxo groups on a ring sulfur;

each R^{6a} is independently selected from C_{1-6} aliphatic, halo, alkoxy, or amino;

each R^{6b} is independently selected from C_{1-3} aliphatic or $-N(R^7)_2$, and two R^{6b} on the same or an adjacent carbon optionally are taken together with the intervening carbon(s) to form a 5-6 membered ring having 1-2 ring heteroatoms selected from N, O or S;

W is –Q-, –Q-C(O)-, $-C(R^9)_2-C(R^9)(R^{12})-$, or $-C(R^9)_2-[C(R^9)(R^{12})]_2-$;

Q is $-C(R^9)_2-$ or $-C(R^9)_2C(R^9)_2-$;

G is –OH, $-NR^4R^5$, $-N(R^9)CONR^4R^5$, $-N(R^9)SO_2(C_{1-3}$ aliphatic), $-N(R^9)COCF_3$, $-N(R^9)CO(C_{1-6}$ aliphatic), $-N(R^9)$CO(heterocyclyl), $-N(R^9)$CO(heteroaryl), $-N(R^9)$CO(aryl), a 3-7 membered heterocyclyl ring, or a 5-6 membered heteroaryl, wherein each of the heteroaryl, aryl and heterocyclyl moieties of G is optionally substituted by 1-3 R^{10};

R^1 is hydrogen, halo, C_{1-3} aliphatic, amino, cyano, $(C_{1-3}$ alkyl$)_{1-2}$ amino, C_{1-3} alkoxy, $-CONH_2$, $-NHCOCF_3$, or $-CH_2NH_2$;

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R^2 is hydrogen, halo, C_{1-3} aliphatic, $-CF_3$;

R^3 is hydrogen, halo, C_{1-6} aliphatic, C_{1-6} haloalkyl, C_{1-6} alkoxy, hydroxy, amino, cyano, or $(C_{1-6}$ alkyl$)_{1-2}$ amino;

R^4 is hydrogen, 3-7 membered heterocyclyl, or C_{1-6} aliphatic;

R^5 is hydrogen, C_{1-6} aliphatic group or a 3-7 membered heterocyclic ring having 1-2 ring heteroatoms selected from N, O, or S, wherein R^5 is optionally substituted by halo, $-OR^7$, -CN, $-SR^8$, $-S(O)_2R^8$, $-S(O)_2N(R^7)_2$, $-C(O)R^7$, $-CO_2R^7$, $-N(R^7)_2$, $-C(O)N(R^7)_2$, $-N(R^7)C(O)R^7$, $-N(R^7)CO_2R^8$, or $-N(R^7)C(O)N(R^7)_2$;

each R^7 is independently selected from hydrogen or C_{1-4} aliphatic, or two R^7 on the same nitrogen atom are taken together with the nitrogen to form a 5-6 membered heteroaryl or heterocyclyl ring;

each R^8 is independently selected from C_{1-4} aliphatic;

each R^9 is independently selected from hydrogen or C_{1-3} aliphatic;

each R^{10} is independently selected from oxo, $-R^{11}$, $-T-R^{11}$, or $-V-T-R^{11}$;

each R^{11} is independently selected from C_{1-6} aliphatic, halo, $-S(O)_2N(R^7)_2$, $-OR^7$, -CN, $-SR^8$, $-S(O)_2R^8$, $-C(O)R^7$, $-CO_2R^7$, $-N(R^7)_2$, $-C(O)N(R^7)_2$, $-N(R^7)C(O)R^7$, $-N(R^7)CO_2R^7$, or $-N(R^7)C(O)N(R^7)_2$;

T is a straight or branched C_{1-4} alkylene chain;

V is –O-, $-N(R^7)-$, -S-, -S(O)-, $-S(O)_2-$, -C(O)-, or $-CO_2-$; and

R^{12} is hydrogen, C_{1-6}aliphatic, substituted or unsubstituted phenyl, substituted or unsubstituted benzyl, or an amino acid side chain.

Claims 2-8. (Canceled)

9. (Currently Amended) The compound of claim 1 8 where the –W-G or $-C(R^9)_3$ substituent on Ring A is ortho to the position where the beta-carboline portion is attached.

Claims 10-16. (Canceled)

17. (Original) A pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier.

18. (Canceled)

19. (Withdrawn) A method of treating an IKK-mediated disease comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 1.

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20. (Withdrawn) The method of claim 19 wherein the disease is an inflammatory disease or an immune-related disease.

21. (Withdrawn) The method of claim 19 wherein the disease is selected from the group consisting of rheumatoid arthritis, asthma, psoriasis, psoriatic arthritis, chronic obstructive pulmonary disease, inflammatory bowel disease or multiple sclerosis.

22. (Withdrawn) The method of claim 19 wherein the disease is cancer.

23. (Withdrawn) The method of claim 22 wherein the cancer is selected from lymphoma, multiple myeloma, osteolytic bone mestasis, head or neck cancer, lung cancer, prostate cancer or pancreatic cancer.

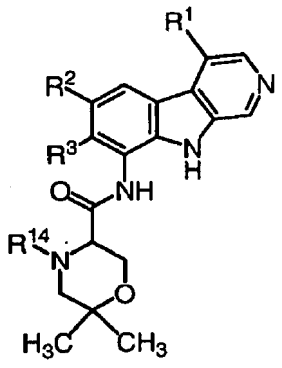
24. (Withdrawn) The method of claim 23 wherein the cancer is a lymphoma.

25. (Withdrawn) A method of inhibiting IKK in a patient in need thereof comprising administering to the patient a compound of claim 1.

Claim 26 (Canceled).

Claim 27 (Canceled).

28. (Original) A compound of formula IV:



IV

where R^{14} is an amino protecting group or hydrogen;

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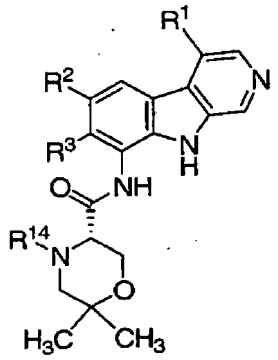
R^1 is hydrogen, halo, C_{1-3} aliphatic, amino, cyano, $(C_{1-3}$ alkyl$)_{1-2}$ amino, C_{1-3} alkoxy, $-CONH_2$, $-NHCOCF_3$, or $-CH_2NH_2$;

R^2 is hydrogen, halo, C_{1-3} aliphatic, $-CF_3$; and

R^3 is hydrogen, halo, C_{1-6} aliphatic, C_{1-6} haloalkyl, C_{1-6} alkoxy, hydroxy, amino, cyano, or $(C_{1-6}$ alkyl$)_{1-2}$ amino.

29. (Currently Amended) The compound of claim 28 ~~that is~~ , wherein the compound is represented by formula (*S*)-IV:



30. (Withdrawn) A method of treating an inflammatory disease or an immune-related disease comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 1.

31. (Withdrawn) The method of claim 30 wherein the disease is selected from rheumatoid arthritis, asthma, psoriasis, psoriatic arthritis, chronic obstructive pulmonary disease, inflammatory bowel disease or multiple sclerosis.

32. (Withdrawn) A method of treating cancer comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 1.

33. (Withdrawn) The method of claim 32 wherein the cancer is selected from lymphoma, multiple myeloma, osteolytic bone mestasis, head or neck cancer, lung cancer, prostate cancer or pancreatic cancer.

34. (Withdrawn) The method of claim 33 wherein the cancer is a lymphoma.

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RESPONSE

With this response, claims 2-8, 10-16, 18, 26, and 27 have been canceled, and claims 1, 9, and 29 have been amended. Claims 1, 9, 17, 28, and 29 are currently pending and claims 19-25 and 30-34 are withdrawn. Applicants reserve the right to pursue the subject matter of any canceled claims in continuation or divisional applications.

Claim Objections

1) The Examiner has objected to claims 1, 8, 9, and 16-18 as containing non-elected subject matter. Applicants have amended the claims to contain only elected subject matter and thus Applicants respectfully submit that the objection be withdrawn.

2) The Examiner has objected to claims 12 and 13 as being of improper dependent form for failing to further limit the subject matter of a previous claim, specifically claim 11. Applicants have canceled claims 12 and 13 and thus the rejection is now moot. Applicants have, however, amended claim 1 to recite "R^{12} is hydrogen, C_{1-6}aliphatic, substituted or unsubstituted phenyl, substituted or unsubstituted benzyl, or an amino acid side chain". Support for this amendment can be found on pages 15 and 16 of the specification as filed.

Rejection under 35 U.S.C. 112, second paragraph:

1) The Examiner has rejected claims 11-13 and 15 and asserts that the terms "having", used in the definitions of the compounds in the claimed process, renders the products indefinite and states that forms of the term "having" can be considered open ended language and is therefore including additional subject matter in the compounds of the claims that is not described in the instant specfiication and is not particularly pointed out or distinctly claimed.

Applicants respectfully disagree and point out that claims 11-13 and 15 are directed to compound claims (not process claims as the Examiner asserts) and the term "having" is used to further define a particular chemical formula (e.g., a compound of claim 10 having the formula III-A) and is not being used to claim compounds not described in the specification. Although Applicants traverse the Examiner's rejection, in an effort to expedite prosecution, Applicants have canceled claims 11-13 and 15 and thus the rejection is now moot.

2) The Examiner has rejected claims 1, 8-11, and 17 and states that the phrase "amino acid side chain" renders the claims indefinite as it is unclear what substitutents are considered "amino acid side chains". The Examiner further states that it is unclear what are "amino acid side chains" as there is no guidance on how to determine if a substituent is an "amino acid side chain".

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Applicants respectfully disagree and submit that one of ordinary skill in the art can readily determine what an amino acid side chain is. It is well-known (see, for example, the textbook "Biochemistry", Stryer, ed., 3rd ed., W. H. Freeman and Company, New York (1988)) that the structure of amino acids consists of "an amino group, a carboxyl group, a hydrogen atom, and a distinctive R group bonded to a carbon atom, which is called the α-carbon atom because it is adjacent to the carboxyl (acidic group)." It is further stated in Stryer that "an R group is referred to as a side chain..." Because amino acid structure is so well known, one of ordinary skill in the art, having an understanding of general amino acid structure, would readily be able to ascertain what the amino acid side chain is for a natural or unnatural amino acid by simply looking at the structure of the amino acid. Stryer also describes the 20 known natural amino acids and describes the properties of each of the side chains.

In view of the arguments presented above, Applicants respectfully submit that the term "amino acid side chain" is indeed definite and respectfully request that the rejection be withdrawn.

3) The Examiner has rejected claim 29 and states that claim 29 does not provide what (S)-IV is and does not stand alone to define the invention as it is unclear what (S)-IV is .

In an effort to clarify the scope of claim 29, Applicants have amended claim 29 to include the formula of (S)-IV showing the (S) stereochemistry for the compound of formula (IV). Applicants thus respectfully request that the rejection be withdrawn.

Provisional nonstatutory obviousness-type double patenting rejection:

The Examiner has provisionally rejected claims 1, 8-15, and 17 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-19 of copending Application No. 11/101,998.

Applicants will address this rejection when allowable subject matter is indicated for the instant claims.

Rejection under 35 U.S.C. § 103(a):

The Examiner has rejected claims 1, 8, 9, and 17 as being unpatentable over Castro *et al.* Specifically, the Examiner states that the difference between the prior art and the claims at issue is that the prior art provides an unsubstituted ring A, but ring A of the instant claims is substituted by at least one of $C(R^9)_3$, W-G, or G, wherein $C(R^9)_3$ can be methyl. The Examiner further states that the substitution of a methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results and that the motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (i.e., inhibitors of IKK).

Applicants respectfully submit that that the Examiner has not established a *prima facie* case of obviousness and thus claims 1, 8, 9 and 17 are not obvious over Castro *et al.*

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As stated in MPEP § 2142, in order to establish a *prima facie* case of obviousness: 1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available in the art, to modify the reference or to combine the teachings; 2) there must be a reasonable expectation of success; and 3) the prior art reference (or references when combined) must teach or suggest all of the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success *must both be found in the prior art, and not based on applicant's disclosure.* MPEP §2142 also states that impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art.

Applicants respectfully submit that there is no suggestion or motivation in Castro *et al.*, alone or combined with knowledge generally available in the art, to modify the reference to arrive at the claimed invention, nor does it provide any reasonable expectation that modification of the morpholine ring to include methyl would successfully yield compounds having activity against IKK that would be useful for the diseases and disorders described by the Applicants.

Specifically, Castro *et al.*, teach away from the use of morpholine substituents. For example, in Table 4 (which lists a variety of analogues prepared along with their activity against IKK), compound **35**, the compound that is cited by the Examiner, has an IC_{50} of greater than 20, whereas other compounds that do not have the morpholine substituent (e.g., compound **33**) have increased activity (0.7 μM for compound **33**). Thus, in view of the disclosure of Castro *et al.*, one of ordinary skill in the art would not be motivated to select the morpholine substituent for modification, nor would they have any reasonable expectation that the use or modification of the morpholine substituent would successfully lead to compounds having increased activity as inhibitors of IKK.

In view of the remarks detailed above, Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) of claims 1, 8, 9, and 17 be withdrawn by the Examiner.